NEWS BRIEFING
Advances in Technology

moderated by:
Irl Hirsch, MD
University of Washington Medical Center
EMBARGO POLICY

• All recordings are for personal use only and not for rebroadcast online or in any format.
• Information presented today in this briefing is under embargo until the end of the formal scientific presentation here at the conference.
• Please consult the top of each press release for embargo dates and times.
• Tweeting is not permitted from the news briefing or any sessions. The Association’s social media team will be monitoring all channels.
First Assessment of the Performance of an Implantable CGM System through 180 Days in a Primarily Adolescent Population with Type 1 Diabetes

Ronnie Aronson, MD, FRCPC, FACE
LMC Diabetes and Endocrinology
Toronto, Ontario, Canada
Presenter Disclosures

• Advisory panel: Novo Nordisk, Sanofi
• Research support: AstraZeneca, Eli Lilly, Valeant, Janssen, Senseonics
Background

• Study Objective
  o Current study designed to evaluate safety and effectiveness of the Eversense XL Continuous Glucose Monitoring (CGM) system in primarily pediatric population up to 180 days.

• Study Significance
  o Eversense CGM is the newest CGM system and is very different from traditional CGM – implantable, lasts up to 180 days, wearable transmitter, on-body vibe alerts.
  o While Eversense has been studied in adults, this was the first study of the system in a pediatric population and the first study of any CGM system in a pediatric population for more than 14 days of continuous wear.
The Eversense CGM System

Fully implantable sensor for long term continuous wear up to 180 days

- Wearable transmitter is lightweight and water-resistant
- Wearable transmitter can be taken on/off without replacing sensor
- Patient is alerted when low or high glucose or before going low or high
- Low and high glucose alerts on-screen via the mobile app or on-body via transmitter vibrations
- Gentle-on-skin adhesive
Study Design

- Prospective, unblinded, single-arm, single-center
- N = 36 participants
  - 30 peds (>11yo, mean 14yo)
  - 6 adults
- 180-day duration

**Primary outcomes:**
- Performance: Accuracy and longevity over 180 days
- Safety: Safety over 180 days, plus removal and follow-up

**Methods:**
- Sensor insertion at day 0 and removal at day 180 (done in clinic during in-office procedure visit)
- Home use from days 1-180
- In-clinic accuracy vs. YSI assessments (every 30 days)
Accuracy

- Mean absolute relative difference (MARD) as standard accuracy metric
  - The difference between sensor vs. reference glucose value
  - The smaller the number the more accurate
- Generally <10% MARD is considered highly accurate
- Eversense MARD = 9.4%
Accuracy (cont’d)

<table>
<thead>
<tr>
<th>Zone</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6688</td>
<td>93.4%</td>
</tr>
<tr>
<td>B</td>
<td>447</td>
<td>6.2%</td>
</tr>
<tr>
<td>C</td>
<td>28</td>
<td>0.4%</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>E</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Total</td>
<td>7163</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Consensus Error Grid Plot

Test device glucose (mg/dL)

Reference glucose (mg/dL)
Safety

- No serious adverse events related to insertion/removal, nor device
- Insertion and removal procedures and the device itself were well-tolerated
- No infections observed
- Mild skin reactions to the sensor that fully resolved within 2-8 weeks of removal
- Limited skin reactions to transmitter adhesive
Summary

• Comparable accuracy to marketed CGMs
  o MARD of 9.4%
  o 99.6% of data in zones A and B of consensus error grid
  o 15/15% metric of 83%, through 180 days, in primarily pediatric population

• Strong safety performance and well tolerated

• Pediatric population favorably rated
  o Long sensor life, implanted wear and vibratory alerts
Conclusion

Eversense CGM system

• Provides a safe and durable alternative to currently available CGM systems, with proven accuracy in a pediatric population
• Insertion and removal procedures are well-tolerated and safe
• Patients show a high degree of likeability to its specific features
### 15 year old male subject with T1D x 14 yr insulin pump & prior CGM user

<table>
<thead>
<tr>
<th>Baseline</th>
<th>180 Days</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>8.5%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Time in range (70-180 mg/dL)</td>
<td>55.2%</td>
<td>62.7%</td>
</tr>
<tr>
<td>Hypoglycemia (&lt;70 mg/dL)</td>
<td>4.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hyperglycemia (&gt;180 mg/dL)</td>
<td>40.3%</td>
<td>36.3%</td>
</tr>
</tbody>
</table>

**What I liked best:**
“I liked that it stays in for 180 days not like the others where it has to be replaced every week.”

### 14 year old female subject with T1D x 6 yr insulin pump & prior CGM user

<table>
<thead>
<tr>
<th>Baseline</th>
<th>180 Days</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>7.0%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Time in range (70-180 mg/dL)</td>
<td>57.6%</td>
<td>66.0%</td>
</tr>
<tr>
<td>Hypoglycemia (&lt;70 mg/dL)</td>
<td>1.5%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Hyperglycemia (&gt;180 mg/dL)</td>
<td>40.9%</td>
<td>33.6%</td>
</tr>
</tbody>
</table>

**What I liked best:**
“When on sports field, you could monitor BG levels so you could be more proactive than reactive.”
Safety and Performance of the Omnipod Hybrid Closed-Loop System in Adults with Type 1 Diabetes Over 5 Days Under Free-Living Conditions

Bruce Buckingham, MD
Stanford University
Presenter Disclosures

• Research funding from Insulet Corp., Medtronic, Tandem, Dexcom, NIH and Helmsley Foundation

• Advisory board member for NovoNordisk and Convatec
Study Overview

Background
• The Omnipod personalized Model Predictive Control algorithm has been tested in 2 safety and feasibility studies in 82 adult, adolescent, and pediatric patients

Study Design
• 5 day/4 night hybrid closed-loop hotel study with free-living conditions
  o Unrestricted meals
  o Daily moderate-intensity exercise
• 7 days of standard therapy data collected
• 11 Adults
  o Mean age 29 yr, diabetes duration 15 yr
  o Mean HbA1c 7.4 ± 1.2%
  o Current therapy MDI (n=3) or CSII (n=8)

Investigational Device. Limited by Federal (or United States) law to investigational use.
## Glycemic Outcomes Overall

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hybrid Closed-Loop Overall (96 h)</th>
<th>Standard Therapy Overall (7 d)</th>
<th>P-Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean glucose, mg/dL</td>
<td>150 ± 11</td>
<td>156 ± 29</td>
<td>0.46</td>
</tr>
<tr>
<td>Time in range, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 mg/dL</td>
<td>1.9 ± 1.3</td>
<td>5.1 ± 4.8</td>
<td>0.001*</td>
</tr>
<tr>
<td>70-180 mg/dL</td>
<td>73.7 ± 7.5</td>
<td>62.5 ± 16.0</td>
<td>0.02*</td>
</tr>
<tr>
<td>&gt;180 mg/dL</td>
<td>24.5 ± 7.7</td>
<td>32.3 ± 18.1</td>
<td>0.12</td>
</tr>
<tr>
<td>≥250 mg/dL</td>
<td>4.5 ± 4.2</td>
<td>8.5 ± 9.1</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

†Calculated using the two-tailed Wilcoxon signed rank test for paired observations; *p<0.05

Data are mean±SD; N=11; outcomes based on sensor glucose
## Glycemic Outcomes Overnight

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hybrid Closed-Loop Overnight (23:00-07:00)</th>
<th>Standard Therapy Overnight (23:00-07:00)</th>
<th>P-Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean glucose, mg/dL</td>
<td>152 ± 32</td>
<td>156 ± 39</td>
<td>0.46</td>
</tr>
<tr>
<td>Time in range, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 mg/dL</td>
<td>0.7 ± 1.1</td>
<td>5.7 ± 7.4</td>
<td>0.02*</td>
</tr>
<tr>
<td>70-180 mg/dL</td>
<td>73.9 ± 21.0</td>
<td>60.7 ± 21.8</td>
<td>0.03*</td>
</tr>
<tr>
<td>&gt;180 mg/dL</td>
<td>25.3 ± 21.2</td>
<td>33.6 ± 23.5</td>
<td>0.28</td>
</tr>
<tr>
<td>≥250 mg/dL</td>
<td>6.1 ± 10.9</td>
<td>8.6 ± 14.1</td>
<td>0.30</td>
</tr>
</tbody>
</table>

†Calculated using the two-tailed Wilcoxon signed rank test for paired observations; *p<0.05
Data are mean±SD; N=11; outcomes based on sensor glucose
Comparison of 24-hr Sensor Glucose for Hybrid Closed-Loop and Standard Therapy

Significant improvements with hybrid closed-loop compared to standard therapy

- Increased time in target range (70-180 mg/dL)
  - 11.2% higher overall
  - 13.2% higher overnight

- Decreased time in hypoglycemia (<70 mg/dL)
  - 3.2% lower overall
  - 5% lower overnight

Results are median (IQR)
Conclusions

• The Omnipod personalized Model Predictive Control (MPC) algorithm was safe and performed well over 5 days of use in adults with type 1 diabetes under free-living conditions
  o Unrestricted meals
  o Moderate-intensity exercise

• Glucose control was maintained in the target range for 74% of time overall, with significant reductions in time spent in hypoglycemia and hyperglycemia compared to standard therapy

• Additional longer-term studies will evaluate the Omnipod MPC algorithm under free-living conditions with extended use in patients of all ages with type 1 diabetes
Artificial Intelligence to Safely Automate Insulin Decisions

12-week Home Use of Hybrid Closed-loop Insulin Delivery System vs. Sensor-assisted Pump Therapy in Adults with Type 1 Diabetes: Intermediate Results of the Multicentre Randomised Crossover Diabeloop WP7 Trial

Sylvia Franc, MD
Sud Francilien Hospital

On behalf of the DIABELOOP Consortium:
Presenter Disclosures

• Medical director and vice-president of CERITD (Centre of Study and Research on intensification of treatment of Diabetes)
• Board Member: NovoNordisk, Roche, Sanofi
• Speaker : Lilly, NovoNordisk
• Research Support: MSD, Dexcom
• Stock/Shareholder: Diabeloop SA
Living with Diabetes Type 1 is a Major Burden

High expectations from patients

If the Artificial Pancreas was available today, in what extent would you like to benefit from it now?

>1.5 million people living with T1 diabetes in US
Number increasing by ~4% per year

Anyone can develop T1D; 50% of cases start before age 20
Patients have to make about 30 therapeutic decisions per day

83% patients would like to benefit from it now

2014 survey from the French Diabetes Association (n=738 patients)
The DBLG1 “Closed-loop” System of Diabeloop

Personalized algorithm settings:
- Targets
- Reactivities
- Meals, physical activities, special events

Artificial intelligence to safely automate insulin delivery decisions
Where were we at ADA in 2017?
Diabeloop system tested in difficult situations

T 70-180 (full day): 80.5% vs. 54%

T 80-140 Night: 59.7% vs. 22.4%
= ~3x as much time spent in the target range

In case of heavy meals with much fat and proteins intake, even expert patients were unable to control hyperglycemia

3 Heavy meals
1 Japanese Restaurant
2 French Gastronomic Restaurant
3 Italian Pizza/Tiramisu Restaurant

S Franc ADA 2017
Diabeloop 2018 - Where Are We Now?

Assessment of the Diabeloop system at home over a 12 week period; real-life conditions, no restrictions

67 patients:
- 33 with Diabeloop
- 34 with their usual pump and Dexcom CGM
- During 12 weeks
- In 12 centers across France:

![Map of France with centers marked]

![Graph showing sensor glucose levels over time for Open Loop (N=34) and Closed Loop (N=33)]
Diabeloop: Results at 12 Weeks

Outstanding Time in Target

<table>
<thead>
<tr>
<th>Range 70-180 mg/dl</th>
<th>Open Loop</th>
<th>Closed Loop</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.0001</td>
<td>56.6%</td>
<td>69.3%</td>
</tr>
</tbody>
</table>

- + 12.7% time in the target range = + 3h per 24h

Decrease in Hypo: Avoids Severe Discomfort

<table>
<thead>
<tr>
<th>% time &lt; 70 mg/dl</th>
<th>Open Loop</th>
<th>Closed Loop</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.001</td>
<td>4.5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

- - 2.5% time in hypoG = - 36 mn per 24h

Drop in Average Glycemia: Less Complications

<table>
<thead>
<tr>
<th>Mean BG values</th>
<th>Open Loop</th>
<th>Closed Loop</th>
</tr>
</thead>
<tbody>
<tr>
<td>168.5 mg/dl</td>
<td>P= 0.012</td>
<td>156 mg/dl</td>
</tr>
</tbody>
</table>

- -12 mg/dL: drop in average glycemic level

Drop in Nocturnal Hypo

<table>
<thead>
<tr>
<th>% time &lt; 70 mg/dl</th>
<th>Open Loop</th>
<th>Closed Loop</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.0001</td>
<td>3.9%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

~3 x less time in hypos during the night

At NIGHT
A System That Truly Benefits the Patients: Outstanding Feedback from Clinical Trials

- A better blood glucose control, less hypoglycemia
- A better quality of life: patients can be more serene and active
- Diabeloop adapts to patient’s life thanks to:
  - **Customization** capability of the AI enriched system
  - **Telemedicine** capabilities

“A big thank you from my family who was finally able to sleep peacefully.”

“Diabeloop’s system makes things so much easier. It prevents me from waking up at nights with hyperglycemia, or sweating from hypoglycemia.”

“It changed my family’s life and mine: canyoning, swimming, solo walks, after work drinks and riding, just like everyone! A pure moment of happiness!”
Insulin-plus-Pramlintide Artificial Pancreas in Type 1 Diabetes Randomized Controlled Trial

Ahmad Haidar, PhD
McGill University, Montreal, Canada
Funding: Juvenile Diabetes Research Foundation
Presenter Disclosures

• Owns IP in the field of artificial pancreas
• Received consulting and IP purchase fees from Eli Lilly
Insulin-Alone Artificial Pancreas

- Insulin-alone artificial pancreas systems improve glucose control compared to conventional pump therapies
- However, post-meal control remains a challenge
Pramlintide

- Is an analog of amylin
- Is lost in type 1 diabetes
- Slows gastric emptying
- Suppresses glucagon secretion
- Promotes satiety
- Improves glucose control in type 1 diabetes

Does a dual-hormone artificial pancreas that delivers insulin and pramlintide improve glucose levels compared to an insulin-only artificial pancreas?
Randomized Controlled Trial

• We conducted a clinical trial in adults with type 1 diabetes. Each participant underwent three, 24-hr experiments with their glucose levels controlled with each of the systems:
  
  o Regular insulin plus pramlintide artificial pancreas
  o Rapid insulin plus pramlintide artificial pancreas
  o Rapid insulin artificial pancreas

• Two pumps
## Results

<table>
<thead>
<tr>
<th></th>
<th>Rapid Insulin</th>
<th>Rapid Insulin + Pramlintide</th>
<th>Regular Insulin + Pramlintide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time spent between 3.9 and 10.0 mmol/L period (%)</td>
<td>74 P=0.001</td>
<td>86</td>
<td>68 P=0.36</td>
</tr>
<tr>
<td>Mean glucose level (mmol/L)</td>
<td>7.9 P=0.01</td>
<td>7.4</td>
<td>7.9 P=0.79</td>
</tr>
<tr>
<td>Coefficient of Variance (%)</td>
<td>31 P=0.017</td>
<td>27</td>
<td>33 P=0.18</td>
</tr>
</tbody>
</table>
Starting glucose level below 90 mg/dL

Starting glucose level above 180 mg/dL

Starting Glucose Level Between 90 and 180 mg/dL
Conclusions

• A dual-hormone artificial pancreas delivering rapid insulin and pramlintide improves glucose control and reduces glucose variability compared to insulin-alone, first-generation, artificial pancreas
• Longer and larger studies in free-living outpatient settings are warranted
EMBARGO REMINDER

• Any reporters in violation of the embargo policy will be barred from this and future Scientific Sessions.
• For interviews with any of the presenters, please contact Michelle Kirkwood or a member of the Press Office team.
MEDIA CONTACT

On-site Press Office – Room 109B

Press@diabetes.org